activity of nAChRs. Our findings open a new scenario in understanding of purinergic regulation.

SENSITIVITY OF HIPPOCAMPAL SLICES OF NEWBORN RATS WITH PRENATAL HYPERHOMOCYSTEINEMIA TO 4-AMINOPYRIDINE-INDUCED SEIZURE-LIKES EVENTS

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Homocysteine, a thiol-containing amino acid derived from dietary methionine through demethylation. The breakage of metabolism due to genetic alteration in metabolic enzymes or deficiency in cofactors may lead to hyperhomocysteinemia. Abnormal accumulation of homocysteine during pregnancy induces learning deficits in offspring at early postnatal development. It was shown, that HHCy can contribute to seizures in patients with Down syndrome, depression and in alcohol withdrawal. The goal of this study was to estimate the sensitivity of hippocampal slices of newborn rats with prenatal hyperhomocysteinemia (pHHCy) to 4-aminopyridine–induced seizure-likes events (SLE). Experiments were performed on slices of Wistar rats during second and third postnatal weeks (P9-19) using extracellular field electrodes in the CA3 pyramidal cell layer of hippocampus. To determinate the threshold of 4-aminopiridine for generation of SLE the convulsant was added by increasing doses. Pups with pHHCy were born from females received daily methionine with food. In control group application of 15-35 μM 4-aminopyridine induced a gradual increase of the frequency of multiunit activity of hippocampus neurons. In concentration of 50-75 μM 4-aminopyridine induced SLE in 75% cases (n=15) after 4.3±0.9 min of perfusion. In slices prepared from the hippocampus of rats with pHHCy the elevation of background neuronal firing was observed and application of 15-35 μM 4-aminopyridine induced SLE in 88% of the cases with 6.0±0.6 min of seizure onset (n=26). Our findings indicate that pHHCy significantly lowers the threshold of 4-aminopyridine–induced SLE. It is known that homocysteine and its metabolites are potent agonists of NMDA-receptor, which are linked with epileptogenesis. It is possible that pHHCy can induce the hyperexcitability of neuronal network of immature hippocampus by stimulating NMDA-receptors and changing the electrophysiology property of neurons.

This work was supported by RSF № 14-15-00618.